

# The Pattern of Histopathology of Gall Bladder of Patients Undergoing Cholecystectomy

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## ABSTRACT

**Background:** Cholecystitis accounts for high mortality and morbidity, with most appropriate treatment being surgical removal of the gallbladder. There seems to be specific need for histopathology of gall bladder, as selective approach for sending cholecystectomy specimens for histopathology can result in missing discrete pathologies such as premalignant lesions like porcelain gallbladder, carcinoma-in-situ, and early carcinomas. Hence it is appropriate to study the pattern of histopathology of gall bladder in patients undergoing cholecystectomy.

**Methodology:** Present study was conducted in Department of Surgery and Pathology, with all patients undergoing open or laparoscopic cholecystectomy. The pattern of response in the gall bladder mucosa was studied. Three sections including neck, body and fundus of gall bladder specimen were obtained.

**Results:** Forty seven patients with symptomatic gallstones were admitted with a female to male ratio of 3:1. The age ranged from 21 to 80 years with a mean age of  $45 \pm 5$  years, most of the patients were in the age group of 51-60 years. The most common findings were of chronic cholecystitis (70.2%), followed by chronic follicular cholecystitis (12.7%). All samples collected showed congestion, whereas edema was found in 46 samples and ulceration was found in 45 samples.

**Conclusion:** To conclude, our study showed that females were more effected from cholecystitis and underwent cholecystectomy. The most common histopathological finding in our study was of chronic cholecystitis followed by chronic follicular cholecystitis. There were no signs or symptoms suggestive or underlying malignancy in any patient.

**Key words:** Gall Bladder, Gallstones, Cholecystitis, Cholelithiasis.

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## INTRODUCTION

Cholecystitis accounts for 3–10% of cases of abdominal pain worldwide with the highest frequency in people aged 50–69 years old.<sup>1</sup> Cholecystitis causes an estimated 0.65 million emergency department visits, 0.39 million hospital admissions and a mortality rate of 0.7 per 10000 in the US in 2012.<sup>2</sup> Biliary colic often precedes cholecystitis, patient experiences sever pain, while in cholecystitis the pain becomes more severe and constant.<sup>3,4</sup> Lack of proper treatment results in recurrent episodes of cholecystitis and could result in gall stone pancreatitis, common bile duct stones, or inflammation of common bile duct.<sup>4,5</sup> Certain factors are associated with risk of developing gall stones which include birth control pills, pregnancy, and a family history of gallstones, obesity, diabetes, liver disease, or rapid weight loss.<sup>6</sup>

The most appropriate treatment for cholecystitis is surgical removal of the gallbladder (laparoscopic cholecystectomy).<sup>4</sup> Cholecystectomy for benign gallbladder diseases can lead to previously undiagnosed gallbladder cancer during histopathological evaluation. Despite some controversy over its usefulness, histopathological evaluation of all gallbladder specimens is common in most hospitals.<sup>7</sup> There seems to be specific need for histopathology of gall bladder as selective approach for sending cholecystectomy specimens for histopathology can result in missing discrete pathologies such as premalignant benign lesions like porcelain gallbladder, carcinoma-in-situ, and early carcinomas.<sup>8</sup> Early carcinoma of gallbladder notoriously remains undiagnosed without histopathology as it

neither produces clinical symptoms or signs nor provides any clues on ultrasound assessment. Cholecystectomy performed with provisional diagnosis of benign diseases based on clinical, ultrasonological and computerized tomographic scanning misses a significant number of early malignant lesions of gallbladder. To avoid such fallacies, therefore, every cholecystectomy specimen should be routinely examined for histopathology.<sup>9</sup> Histopathology is restricted to only those specimens, which show gross abnormalities. This practice is based on the assumption that gallbladder carcinoma is always associated with macroscopic abnormalities. The histopathological features and incidence of gall bladder lesion varies depending on races, countries, and institutes. Hence this study was designed to study the results of routine pathology of the gallbladder after cholecystectomy for benign gallbladder diseases with regard to unexpected primary gallbladder cancer (UPGC).

## MATERIALS AND METHODS

This observational study was conducted in collaboration of Department of Surgery and Pathology for a period of two months May-June 2017 after approval from Institutional Ethics Committee. All patients admitted to Surgery Department undergoing cholecystectomy procedure were included in the study if they were willing to give written informed consent. All patients who underwent previous abdominal surgery were excluded from the

study. All patients undergoing open or laparoscopic cholecystectomy, following the procedure the excised gallbladder was sent to the pathology department in 10% neutral buffered formalin. After overnight fixation, gross examination was conducted and tissue bits were taken one from neck body and fundus respectively if grossly normal and more from representative site if any gross abnormality detected. The pattern of response in the gall bladder mucosa such as type of inflammation, cholesterolosis, mucocele, hyperplasia, metaplasia, dysplasia and malignant changes was studied with regard to number, size, weight, volume and morphological type of the stone(s). Four sections including the entire wall were obtained; two from the body and one each from the fundus and neck of the gall bladder. Additional sections were taken from abnormal appearing mucosa.

Sections were stained with hematoxylin and eosin stain (H & E). The various morphological responses were then categorized under four broad categories – cholecystitis, hyperplasia, metaplasia and carcinoma.

### Statistical Analysis

The data was tabulated as mean  $\pm$  standard deviation (SD). Results were analyzed using non parametric tests (Chi-Square Test), parametric tests (two tailed student t-test) and correlation (Pearson correlation coefficients) analysis. A  $p < 0.05$  was considered statistically significant.

**Table 1: Staining Procedures**

<b>H &amp; E</b>	Hematoxylin—basic dye, binds acidic nucleic acids - blue-purple Eosin—acidic dye, binds basic/ negatively charged structures-cytoplasm/ muscle/ connective tissue cationic amino groups on proteins- pink/ orange/ red With an H & E stain, mucus and cartilage will stain a light blue color.
<b>Sudan Stains -</b>	Lipids, Phospholipids
<b>Sudan black,</b>	Unconjugated lipids - oil red O, Sudan black, Sudan III, IV , cooper rubeanic acid
<b>Sudan IV, Oil red O.</b>	Free Cholesterol- filipin, Per-chloric acid naphthoquinone(PAN) Cholesteryl esters- Schultz Monoglycerides & triglycerides- Calcium Lipase

## RESULTS

Over a period of two months, forty seven patients with symptomatic gallstones were admitted for cholecystectomy. There were 37 females and 12 males with a female to male ratio of 3:1. The age ranged from 21 to 80 years with a mean age of  $45 \pm 5$  years, most of the patients were in the age group of 51-60 years (31.09%). (Table 2) The histological picture of the patient is shown in Table 3, the most common findings were of chronic cholecystitis

(70.2%), followed by chronic follicular cholecystitis (12.7%). The findings of ulceration, edema and congestion are shown in Table 4. All samples collected showed congestion, whereas edema was found in 46 samples and ulceration was found in 45 samples. Majority of the patients had mild/moderate ulceration ( $n=17$ ), whereas most of the participants had moderate edema ( $n=18$ ) and severe congestion ( $n=17$ ). One patient had no edema and 2 patients had no ulcerations.

**Table 2: Age Distribution of patients**

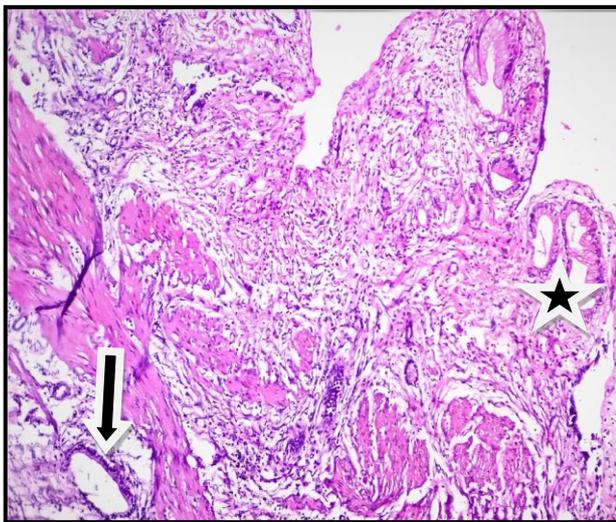
Age of Patients (years)	No. of Patients (%)
21-30	09 (19.14)
31-40	11 (23.40)
41-50	08 (17.02)
51-60	15 (31.09)
61-70	03 (06.30)
71-80	01 (02.10)

**Table 3: Histopathological report of patients**

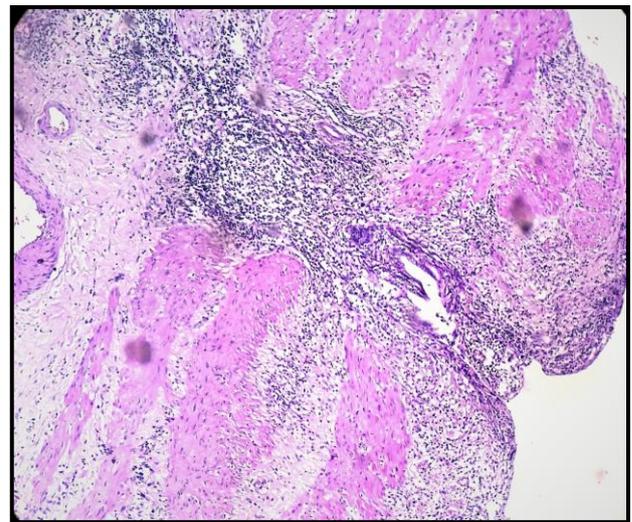
Histopathology	Male	Female	%
Chronic cholecystitis	8	25	70.2
Chronic follicular cholecystitis	1	5	12.7
Chronic active cholecystitis	1	1	4.2
Spongoid hyperplasia		2	4.2
Chronic cholecystitis with fibrosis		2	4.2
Chronic cholecystitis with foamy		2	4.2

**Table 4: Findings in gall bladder**

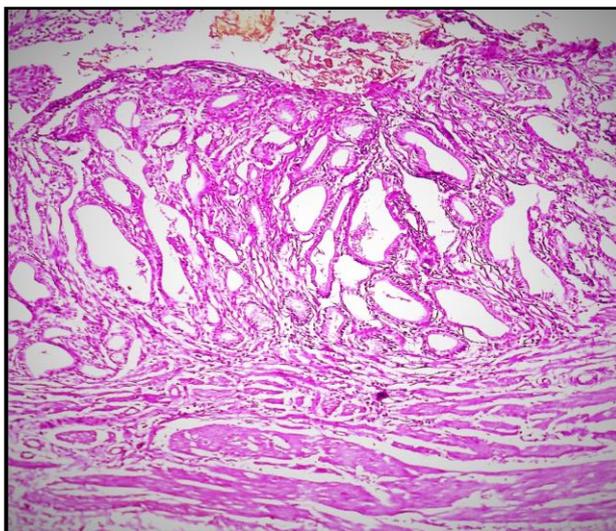
	Ulceration (n)	Edema (n)	Congestion (n)
Mild	17	18	14
Moderate	17	17	16
Severe	11	11	17
Absent	2	1	0



**Fig 1: H& E Stain (10 X magnification): Rokitansky-Aschoff sinuses (herniation of epithelial cells through the fibromuscular layer of the gallbladder wall) in lower left corner (arrow), also shows gastric gland metaplasia (star)**



**Fig 3: H& E Stain (10 X magnification): Follicular cholecystitis**



**Fig 2: H& E Stain (10 X magnification): spongoid hyperplasia of gall bladder mucosa**

## DISCUSSION

In this study, mean age of patient was  $45 \pm 5$  years with the most common histopathological finding in our study of chronic cholecystitis with microscopic examination showing mucosal ulceration, congestion, edema of varying degrees and wall infiltration by chronic inflammatory cells like neutrophils, lymphocytes, macrophages, plasma cells and varying degree of fibrosis. The second most common histopathological finding was chronic follicular cholecystitis with mucosal ulceration, congestion, edema and wall infiltration characterized by the presence of follicles in addition to inflammatory cells like neutrophils, lymphocytes, macrophages, plasma cells and varying degrees of fibrosis. Followed by chronic active cholecystitis with mucosal ulceration, congestion, edema and wall infiltration characterized by presence of eosinophil in addition to inflammatory cells such as neutrophils, lymphocytes, macrophages, plasma cells and varying degrees of fibrosis along with spongoid hyperplasia. Chronic cholecystitis was also associated with metaplasia either intestinal (4 cases) or pyloric gland (5 cases). Mild dysplasia was also seen associated with chronic cholecystitis (10 cases) and moderate

dysplasia (1 case). All patients in our series presented with longstanding history of chronic cholecystitis. There were no signs or symptoms suggestive or underlying malignancy in any patient. A retrospective study of histopathology of cholecystectomy done at a rural government hospital in north India demonstrated that females were predominating over males with a mean age of patients of 44.16±14.64 years. Chronic cholecystitis was most common histopathological entity and metaplasia and xanthogranulomatous cholecystitis was reported in about 6% cases. The results of our study are quite similar to this study as the mean age in our study was 45 years with preponderance of chronic cholecystitis. Though, sex ratio was different as it was 3:1 in our study.<sup>10</sup>

Another cohort study included 220 patients with gallstones for cholecystectomy showed that most of the patients were females in the ratio of 8:1 and majority of the patients presented with chronic cholecystitis. The results are quite similar to our study but in our study the male: female ratio was 1:3 and there was appreciable number of patients with follicular cholecystitis also.<sup>11</sup> One more study done to assess the need for routine histopathology of gallbladder specimens after cholecystectomy demonstrated an average age of 45 years and majority of patients presented with chronic cholecystitis. The results of our study were in similar lines.<sup>12</sup>

Another study to quantify the various outcomes in a tertiary level hospital demonstrated a male: female ratio was 1:2.8 and majority of patients belonging to the age group of 41-50 years and most of them showed chronic calculous cholecystitis followed by chronic cholecystitis. The results of our study are difference from this study as there is more propensity of male preponderance in this study.<sup>13</sup>

There are a few limitations our study, firstly the sample size is small, as this was time based study so we had limit the number of patients. Secondly the duration if the study was small only two months so we had to limit the number of patients as it was one of the projects that had to be completed in a fixed time slot.

## CONCLUSION

To conclude our study showed that females were more affected from cholecystitis and underwent cholecystectomy. The most common histopathological finding in our study was of chronic cholecystitis followed by chronic follicular cholecystitis. There were no signs or symptoms suggestive or underlying malignancy in any patient.

As the histopathological spectrum of gallbladder after cholecystectomy is extremely variable so the protocol of routine histopathology of all gallbladder specimens should be followed to identify the different factors associated with cholecystitis.

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**Conflict of Interest:** None Declared.

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